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09/744,282	04/05/2001	Andreas Martinus Maria Miltenburg	0/98394US	4006

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/744,282	Applicant(s) MILTENBURG ET AL.
	Examiner Phuong Huynh	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/10/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,10-12 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,10-12 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other.

DETAILED ACTION

1. Claims 4-6, 10-12 and 16 are pending. It is noted that Applicant requested the Examiner to disregard the Preliminary Amendment of April 5, 2001. However, if the Examiner were to disregard said amendment, claims 4-15 will not be entered and yet the FOAM mailed 9/10/02 is based on pending claims 4-15. Further, other than the part where the request was to delete "effect" and insert -- effect -- on line 20 and to insert -- , -- after "invention" on line 32 has not been entered, the rest of the said preliminary amendment has been entered. If Applicant wishes to reinstate canceled claims 1-3, it is suggested that Applicant file an amendment to add new claims starting with claim 17 so that the record will be clear. If Applicant wishes the Examiner to disregard the part of the preliminary amendment A that has not been entered as indicated above, please indicates in the next communication.

2. In view of the amendment filed 12/10/02, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 4-6, 10-12 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method of treating an inflammatory autoimmune disease wherein the autoimmune disease is rheumatoid arthritis by inhibiting the reactivity of lymphocytes associated with rheumatoid arthritis, comprising the step of administering a pharmaceutical composition comprising an effective amount of HC gp-39 or a fragment consisting of SEQ ID NO: 6 and a pharmaceutical acceptable carrier, wherein said lymphocytes are reactive to HC gp-39, **does not** reasonably provide enablement for (1) a method of treating rheumatoid arthritis by "**modulating**" the reactivity of lymphocytes associated with said disease, comprising the steps of administering a pharmaceutical composition comprising an effective amount of *any* "**fragments thereof**" of *any* HP gp-39 or *any* fragments such as the ones recited in claims 5, 6, 10, 11 and 12, and a pharmaceutically acceptable carrier, wherein said lymphocytes are reactive to *any* antigens other than HC gp-39 which are present in the same tissue as HC gp-39, and (2) a method of treating *any* "autoimmune disease" by "modulating" the

reactivity of lymphocytes associated with *any* "**autoimmune disease**", comprising the steps of administering a *any* pharmaceutical composition comprising an effective amount of *any* HP gp-39 or *any* fragments thereof, and a pharmaceutically acceptable carrier, wherein said lymphocytes are reactive to *any* antigens other than HC gp-39. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method of treating rheumatoid arthritis by nasal induction tolerance comprising the step of administering a pharmaceutical composition comprising an effective amount of bovine collagen type II HC gp39 (page 10) and a pharmaceutically acceptable carrier (page 14). The specification further discloses HC gp-39 induces the proliferation of PBMC in vitro obtained from some patient with rheumatoid arthritis (See page 15).

The specification does not teach how to make and use *any* HC gp-39 fragments thereof for a method of treating *any* "autoimmune disease" such as rheumatoid arthritis by "modulating" the reactivity of lymphocytes associated with rheumatoid arthritis or any "autoimmune disease" using any HC gp-39 or fragment thereof because there is insufficient guidance as to the structure of any HC gp-39 fragment. Further, there are no guidance and in vivo working as to which "fragment" of HC gp-39 would be useful and effective for treating even rheumatoid arthritis, let alone treating *any* other autoimmune disease. Further, the term "modulating" can be inhibitory or stimulatory and both are mutually exclusive. There is insufficient guidance as to which fragment of H gp-39 is stimulatory or inhibitory for a method of treating *any* autoimmune disease, and *any* autoimmune disease such as rheumatoid arthritis.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion

which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). There is no guidance as to which amino acids within the full-length amino acid sequence of HC gp-39 can be delete and that after deletion would retain the structure and function of the full length HC gp-39, in turn, can be use for treating any autoimmune disease such as rheumatoid arthritis by modulating the reactivity of lymphocyte. Further, the term "modulating" could be stimulatory and/or inhibitory, which is mutually exclusive. The specification discloses only that treating mice nasally with the full length of HC gp-39 inhibits bovine type II collagen-induced rheumatoid arthritis. There is insufficient guidance as to which fragment of HC gp-39 is stimulatory or which fragment of HC gp-39 is inhibitory for a method of treating any autoimmune disease such as rheumatoid arthritis. The term "modulating the reactivity of lymphocytes" is not sufficient to define the biological activity to which the HC gp-39 and fragments thereof which modulation can be inhibitory or stimulatory.

With regard to *any* autoimmune disease, Van Noort *et al*, of record, teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). Given the indefinite number of undisclosed inflammatory autoimmune disease, it is unpredictable which undisclosed fragments of HC gp-39 would be useful for treating any autoimmune disease. Further, other than the specific full length HC gp-39 for treatment of autoimmune rheumatoid arthritis, the specification as filed fails to provide guidance and working example as to whether treatment with the HC gp-39 is appropriate for any other autoimmune disease.

Anderton *et al*, of record, teach peptide-based immunotherapy of autoimmunity is unpredictable and peptides that inhibit autoimmune disease such as encephalomyelitis in vitro actively induce disease in vivo (See page 370, column 1, second full paragraph, bridging column 2, first paragraph, in particular). Further, Anderton *et al* teach clinical trial was suspended due to hypersensitivity reactions in a significant proportion of patients (See page 370, column 2, second paragraph, in particular).

Verheijden *et al* (PTO 1449) teach tolerance can be attained by the amount of autoantigen administered and the **route** of administration is just as important as the autoantigen such as human cartilage glycoprotein-39 (HC gp-39) itself. Verheijden *et al* teach administering a single injection of HC gp-39 in FIA to female BALB/c mice induces clinical signs of arthritis (page 1121, column 2, in particular) whereas intranasal administration of HC gp-39 before

immunization completely abrogated DTH response upon challenge (See page 1122, column 2, last paragraph, in particular).

The Merck manual, of record, does not recognize the use of *any* HC gp-39 fragments thereof for treating *any* inflammatory autoimmune disease such as rheumatoid arthritis (See page 420-421, in particular). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Further, the term "modulating the reactivity of lymphocytes" is not sufficient to define the biological activity to which the HC gp-39 and fragments thereof modulates such as inhibit or stimulated said undefined reactivity. Given the indefinite number of undisclosed "HC pg-39 fragment thereof", a person of skill in the art could not predict which particular amino acid sequence of "HC pg-39" is essential and could be used in a therapeutic method of treating any rheumatoid arthritis, much less for treating any autoimmune disease encompassed by the claim 16. In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients.

With regard to lymphocytes are reactive to *any* antigens other than HC gp-39 which are present in the same tissue as HC gp-39, the specification discloses only lymphocytes are reactive to HC gp-39, the specification does not teach antigens other than HC gp-39 which are present in the same tissue as HC gp-39. Myers *et al*, of record, teach autoimmune response to collagen type II in the CIA models is complex, requiring specific major histocompatibility complex (MHC) molecules, collagen type II specific T cell and B cell immune responses and their associated cytokines (See page 1862, in particular). Myers *et al* teach although the use of altered peptides in the treatment of autoimmune disease such as rheumatoid arthritis is receiving considerable attention as the evidence of their efficacy continues to growth in vitro studies as well as in animal models. However, the development of such therapeutics for human diseases relies upon significant knowledge of the autoantigen (See page 1873, second full paragraph, in particular).

Since the therapeutic indices of the claimed method of treating autoimmune disease can be species- and model-dependent, it is not clear that reliance on one specific model DBA/1 immunized with collagen type II collagen can accurately reflects the efficacy the claimed method for other autoimmune disease. As such, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 12/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 10-12 are not limited to a method for treating, but claim a method for modulating the reactivity of lymphocytes that are reactive to antigens other than HC gp-39 which are present in the same tissue as HC gp-39, (2) the examiner has stated that the invention is enabled for rheumatoid arthritis.

In response to Applicant's arguments, the amended claims still recite "HC gp-39 fragment thereof" and newly added claim 16 is drawn to treating any autoimmune disease. The specification does not teach how to make and use *any* HC gp-39 fragments thereof for a method of treating any "autoimmune disease" including rheumatoid arthritis by "modulating" the reactivity of lymphocytes associated with rheumatoid arthritis or any "autoimmune disease" using any HC gp-39 or fragment thereof because there is insufficient guidance as to the structure of any HC gp-39 fragment. Further, there are no guidance and in vivo working as to which "fragment" of HC gp-39 would be useful and effective for treating even rheumatoid arthritis, let alone treating *any* autoimmune disease. The term "modulating" can be inhibitory or stimulatory and both are mutually exclusive. There is insufficient guidance as to which fragment of HC gp-39 is stimulatory or inhibitory for a method of treating any autoimmune disease such as rheumatoid arthritis. The term "modulating the reactivity of lymphocytes" is not sufficient to define the biological activity to which the HC gp-39 and fragments thereof which modulation can be inhibitory or stimulatory. Given the indefinite number of undisclosed "HC pg-39 fragment thereof", a person of skill in the art could not predict which particular amino acid sequence of "HC pg-39" is essential for stimulatory or which fragment is essential for inhibitory function, in turn could be used in a therapeutic method of treating any autoimmune disease such as rheumatoid arthritis. Further, since the therapeutic indices of the claimed method of treating autoimmune disease can be species- and model-dependent, it is not clear that reliance on one specific model DBA/1 immunized with collagen type II collagen treated with HC gp-39 can accurately reflects the efficacy the claimed method for other autoimmune disease. Even if the method is limited to HC gp-39, the term "HC gp-39" has no structure. As such, it would require

undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

5. Claims 4-6, 10-12 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treating rheumatoid arthritis by "**modulating**" the reactivity of lymphocytes associated with said disease, comprising the steps of administering a pharmaceutical composition comprising an effective amount of *any* "**fragments thereof**" of *any* HP gp-39 or *any* fragments such as the ones recited in claims 6, 10, 11 and 12, and a pharmaceutically acceptable carrier, wherein said lymphocytes are reactive to *any* antigens other than HC gp-39 which are present in the same tissue as HC gp-39, and (2) a method of treating *any* "autoimmune disease" by "modulating" the reactivity of lymphocytes associated with *any* "**autoimmune disease**", comprising the steps of administering a *any* pharmaceutical composition comprising an effective amount of *any* HP gp-39 or *any* fragments thereof, and a pharmaceutically acceptable carrier, wherein said lymphocytes are reactive to *any* antigens other than HC gp-39.

The specification discloses only a method of treating rheumatoid arthritis by nasal induction tolerance comprising the step of administering a pharmaceutical composition comprising an effective amount of bovine collagen type II HC gp39 (page 10) and a pharmaceutically acceptable carrier (page 14). The specification further discloses HC gp-39 induces the proliferation of PBMC in vitro obtained from some patient with rheumatoid arthritis (See page 15).

With the exception of the specific full length HC gp-39, there is insufficient written description about the structure associated with function of (1) *any* "HC gp-39 fragment thereof" for treating (2) *any* autoimmune disease, (3) *any* antigens other than HC gp-30 and (4) *any* method encompassed by claims 4-6, 10-12 and 16 for "modulating" the reactivity of lymphocytes that are reactive to (5) *any* antigens other than HC gp-30 which are present in the same tissue as HC gp-39.

The term "modulating" can be inhibitory or stimulatory and both are mutually exclusive. There is insufficient written description as to which fragment of HC gp-39 is stimulatory or

which fragment of HC gp-39 is inhibitory for a method of treating any autoimmune disease such as rheumatoid arthritis. The term "modulating the reactivity of lymphocytes" is not sufficient to define the biological activity to which the HC gp-39 and fragments thereof which modulation can be inhibitory or stimulatory. Even if the method is limited to HC gp-39, the term "HC gp-39" has no structure. Further, the specification discloses only HC gp-39 for treating only rheumatoid arthritis. Given the lack of a written description of *any* additional representative species of HC gp-39 fragments thereof for a method of treating rheumatoid arthritis, much less for treating any other autoimmune disease by "modulating" undefined reactivity of lymphocytes wherein the modulating activity can be stimulatory or inhibitory, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of autoimmune disease to describe the genus encompassed by the claimed method. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 12/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1 and 4 have been amended and (2) the specification beginning at page 10, line 2 through page 12 line 30 clearly illustrates that treatment with HC-gp-39 can trigger modulatory or regulatory mechanisms that interfere with the induction of arthritis with the use of a non-related antigen.

In response to Applicant's arguments, the amended claims still recite "HC gp-39 fragment thereof" and newly added claim 16 is drawn to treating any autoimmune disease. Further, the specification discloses only a method of treating only rheumatoid arthritis and not any other autoimmune disease by administering only HC gp39 nasally (page 10) and not any other HC gp39 fragment thereof. Even if the method is limited to HC gp-39, the term "HC gp-39" has no structure.

With the exception of the specific full length HC gp-39, there is insufficient written description about the structure associated with function of (1) *any* "HC gp-39 fragment thereof" for treating (2) *any* autoimmune disease, (3) *any* antigens other than HC gp-30 and (4) *any* method encompassed by claims 4-6, 10-12 and 16 for "modulating" the reactivity of

lymphocytes that are reactive to (5) *any* antigens other than HC gp-30 which are present in the same tissue as HC gp-39.

The term "modulating" can be inhibitory or stimulatory and both are mutually exclusive. There is insufficient written description as to which fragment of HC gp-39 is stimulatory or which fragment of HC gp-39 is inhibitory for a method of treating any autoimmune disease such as rheumatoid arthritis. The term "modulating the reactivity of lymphocytes" is not sufficient to define the biological activity to which the HC gp-39 and fragments thereof which modulation can be inhibitory or stimulatory. Even if the method is limited to HC gp-39, the term "HC gp-39" has no structure. Further, the specification discloses only HC gp-39 for treating only rheumatoid arthritis. Given the lack of a written description of *any* additional representative species of HC gp-39 fragments thereof for a method of treating rheumatoid arthritis, much less for treating any other autoimmune disease by "modulating" undefined reactivity of lymphocytes wherein the modulating activity can be stimulatory or inhibitory, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of autoimmune disease to describe the genus encompassed by the claimed method. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 4-6, 10-12 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Verhejiden *et al* (Arthritis and Rheumatism 40(6): 1115-1125, June 1997, PTO 1449).

Verhejiden *et al* teach a method of treating an inflammatory autoimmune disease such as autoimmune rheumatoid arthritis by intranasal administering an effective amount of HC gp-39 in buffer (pharmaceutical acceptable carrier) to a subject prior to immune response, which leads to immunologic nonresponsiveness as measured by DTH assay and suppression of bovine collagen type II induced rheumatoid arthritis upon challenge (See page 1122, column 2, Table 4 and 5, Patients and Methods, in particular). Verhejiden *et al* further teach various fragments of HC gp-39 such as RSFTLASSETGVG, which is 100% identical to the claimed peptide of SEQ ID NO: 6 (See Table 6, in particular). Since the claimed HC gp-39 and fragment are the same as the reference HC gp-39 and fragment, the reference HC gp-39 and HC gp-39 fragment RSFTLASSETGVG are inherently capable of modulating the reactivity of HC gp-39 specific lymphocyte associated with rheumatoid arthritis. Claim 4 is included in this rejection because claims 5-6, 11-12 are depend from claim 4. Claim 16 is included in this rejection because a method of treating a species of autoimmune disease such as rheumatoid arthritis anticipates the claimed genus of autoimmune disease. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 12/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) Applicants have amended the specification to claim proper priority to US Pat No. 5,736,507 which claimed priority to PCT filed Oct 25, 1995 and therefore Verhejiden *et al* is not prior art to the instant patent application.

In response to Applicants' argument, it is noted that "SED ID NO 6 (PTFGRSFTLASSETGVG" in claims 5-6, 11, and 12 has no support in the priority documents EP99/05331 filed 7/19/1999, USSN 08/619,645 filed 3/25/1996 which is now US Pat No. 5,736,507 and EP95/04201 filed 10/25/1995. The filing date of the instant claims 5-6, 11, and 12 is deemed to be the filing date of instant application because (1) the EP99/05331 filed 7/19/1999 is drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)". (2) the USSN 08/619,645, filed 3/25/1996, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the

claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)". (3) The EP95/04201 patent, filed 10/25/1995, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)".

9. Claims 4-6, 10-12 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO 96/13517 (May 1996, PTO 1449).

The WO 96/13517 publication teaches a method of treating an inflammatory autoimmune disease such as autoimmune rheumatoid arthritis by intranasal administering an effective amount of HC gp-39 (page 20, Table 5, in particular) or one or more peptide such as FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR which are identical to the claimed peptide of SEQ ID NO: 1, 2, 3, and 4, respectively (See reference abstract, claims of WO 96/13517 publication, in particular) in PBS, which is a pharmaceutical acceptable carrier to a subject prior to immune response leading to immunologic nonresponsiveness as measured by DTH assay; the reference peptide suppresses bovine type II collagen induced rheumatoid arthritis upon challenge (See page 21, lines 14-19, claims 10, 9, and 4 of WO 96/13517 publication, in particular). Since the claimed HC gp-39 and fragment are the same as the reference HC gp-39 and fragment, the reference HC gp-39 and HC gp-39 fragment RSFTLASSETGVG are inherently capable of modulating the reactivity of HC gp-39 specific lymphocyte associated with rheumatoid arthritis. Claim 4 is included in this rejection because claims 5-6, 11-12 are depend from claim 4. Claim 16 is included in this rejection because a method of treating a species of autoimmune disease such as rheumatoid arthritis anticipates the claimed genus of autoimmune disease. Thus, the reference teachings anticipate the claimed invention.

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Applicants' position is that (1) Applicants have amended the specification to claim proper priority to US Pat No. 5,736,507 which claimed priority to PCT filed Oct 25, 1995 and therefore Verhejiden *et al* is not prior art to the instant patent application.

In response to Applicants' argument, it is noted that "SED ID NO: 6 (PTFGRSFTLASSETGVG" in claims 5-6, 11, and 12 has no support in the priority documents EP99/05331 filed 7/19/1999, USSN 08/619,645 filed 3/25/1996 which is now US Pat No.

5,736,507 and EP95/04201 filed 10/25/1995. The filing date of the instant claims 5-6, 11, and 12 is deemed to be the filing date of instant application because (1) the EP99/05331 filed 7/19/1999 is drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)". (2) the USSN 08/619,645, filed 3/25/1996, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)". (3) The EP95/04201 patent, filed 10/25/1995, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)".

10. Claims 4-6, 10-12 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by the US Pat No. 5,736,507 (April 1998, PTO 892).

The '507 patent teaches a method of treating an inflammatory autoimmune disease such as autoimmune rheumatoid arthritis by intranasal administering an effective amount of HC gp-39 (See entire document, Abstract, column 4, line 26-32, column 7, line 3, in particular) and one or more peptides such as RSFTLASSETGVG, FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR (See reference SEQ ID NO: 6, column 3, in sodium phosphate buffer (PBS, abstract, Table 1, in particular), which is a pharmaceutical acceptable carrier, to a subject prior to immunize with bovine collagen which leads to immunologic nonresponsiveness as measured by DTH assay and suppression of bovine collagen induced rheumatoid arthritis upon challenge (See column 13, lines 6-40, Table 5 and 6, Claims of '507 patent, in particular). Since the claimed HC gp-39 and fragment are the same as the reference HC gp-39 and fragment, the reference HC gp-39 and HC gp-39 fragment RSFTLASSETGVG, are inherently capable of modulating the reactivity of HC gp-39 specific lymphocyte associated with rheumatoid arthritis. Claim 4 is included in this rejection because claims 5-6, 11-12 are depend from claim 4. Claim 16 is included in this rejection because a method of treating a species of autoimmune disease such as rheumatoid arthritis anticipates the claimed genus of autoimmune disease. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 12/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) Applicants have amended the specification to claim proper priority to US Pat No. 5,736,507 which claimed priority to PCT filed Oct 25, 1995 and therefore Verhejiden *et al* is not prior art to the instant patent application.

In response to Applicants' argument, it is noted that "SED ID NO: 6 (PTFGRSFTLASSETGVG" in claims 5-6, 11, and 12 has no support in the priority documents EP99/05331 filed 7/19/1999, USSN 08/619,645 filed 3/25/1996 which is now US Pat No. 5,736,507 and EP95/04201 filed 10/25/1995. The filing date of the instant claims 5-6, 11, and 12 is deemed to be the filing date of instant application because (1) the EP99/05331 filed 7/19/1999 is drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO 6 (PTFGRSFTLASSETGVG)". (2) the USSN 08/619,645, filed 3/25/1996, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO 6 (PTFGRSFTLASSETGVG)". (3) The EP95/04201 patent, filed 10/25/1995, is also drawn to peptides FGRSFTLAS, FTLASSETG, YDDQESVKS, FSKIASNTQ, PTFGRSFTLASSE, VGYDDQESVKSKV, and SQRFSKIASNTQSR, and does not support the claimed limitation "SED ID NO: 6 (PTFGRSFTLASSETGVG)".

11. The following new ground of rejection is necessitated by the amendment filed 12/10/02.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 5-6, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "SEQ ID NO 6(PTFGRSFTLASSETGVG" in Claims 5-6, 11 and 12 represents a departure from the specification and the claims as originally filed. The passages pointed out by applicant in the amendment filed 12/10/02 do not provide a clear support for the said phrase.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located

in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
April 21, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600